

Claims

1. A method of preventing, reducing the extent and/or the severity of secondary ischemic damage in a mammalian organ or tissue, comprising a step of administering an effective amount of an NF- κ B p65 inhibitor to said organ or tissue.
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2. The method according to claim 1, wherein said NF- κ B p65 inhibitor is chosen from the group consisting of: an antisense NF- κ B p65 subunit oligonucleotide; a dominant-negative form of the NF- κ B p65 subunit; a decoy; ribosome inhibitors; enzymatic RNA against NF- κ B p65; and siRNA constructs.
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3. The method according to claim 1, wherein said mammalian organ or tissue is chosen from the group consisting of heart, lungs or lung, kidney, liver, brain, skin, and blood vessels.
4. The method according to claim 3, wherein said organ or tissue is a heart or a section thereof.
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5. The method according to claim 3, wherein said organ or tissue is a brain or a section thereof.
6. The method according to claim 3, wherein the secondary ischemic damage occurs as the result of reperfusion of an organ or tissue following transplantation of said organ or tissue.
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7. The method according to claim 3, wherein the secondary ischemic damage occurs as the result of reperfusion of an organ or tissue following surgical intervention on said organ or tissue or adjacent tissue.
- 25 8. The method according to claim 3, wherein the secondary ischemic damage occurs as the result of reperfusion of the heart following removal of an obstruction in a coronary artery.

9. The method according to claim 1, wherein said NF- κ B p65 inhibitor is an antisense compound from 8 to 40 nucleotides in length, targeted to a nucleic acid molecule encoding NF- κ B p65 subunit or to a fragment or analogue thereof.
- 5 10. The method according to any one of the claims 1 – 9, wherein the antisense NF- κ B p65 subunit oligonucleotide is chosen from the group consisting of SEQ ID NO. 1, SEQ ID NO. 2, and functionally equivalent homologues thereof.
- 10 11. The method according to any one of the claims 1 – 9, wherein the antisense NF- κ B p65 subunit oligonucleotide is SEQ ID NO. 2
12. The method according to any one of the claims 1 – 9, wherein the amount of antisense NF- κ B p65 subunit oligonucleotide administered to the mammal is about 100 μ g to about 5 mg per kg body weight.
- 15 13. The method according to any one of the claims 1 – 9, wherein the ischemia is the result of vascular occlusion of a cardiac vessel
14. The method according to any one of the claims 1 – 9, wherein the ischemia is the result of vascular occlusion of a cerebral vessel
15. The method according to any one of the claims 1 – 9, wherein the ischemia is the result of angioplasty
- 20 16. The method according to any one of the claims 1 – 9, further comprising the step of administering at least one second agent selected from the group consisting of anticoagulants and anti-thrombotics, such as vitamin K-antagonists, heparin and heparinoid agents, platelet aggregation inhibitors and the like.
- 25 17. A method of preventing, reducing the extent and/or the severity of secondary myocardial infarct in a mammalian heart, comprising a step of administering an effective amount of an NF- κ B p65 inhibitor to said heart.

18. A method of protecting tissue adjacent to area of myocardial infarct in a mammal comprising the step of administering an effective amount of an NF- κ B p65 inhibitor locally to the heart of said mammal.
- 5 19. The method according to claim 17 or 18, wherein said NF- κ B p65 inhibitor is chosen from the group consisting of: an antisense NF- κ B p65 subunit oligonucleotide; a dominant-negative form of the NF- κ B p65 subunit; a decoy; ribosome inhibitors; enzymatic RNA against NF- κ B p65; and siRNA constructs.
- 10 20. The method according to claim 17 or 18, wherein said effective amount of an NF- κ B p65 inhibitor is administered locally to the heart.
- 15 21. The method according to claim 17 or 18, wherein said effective amount of an NF- κ B p65 inhibitor is administered locally to the heart within 12 hours, preferably within 8 hours, more preferably within 6 hours, and most preferably within 2 hours from the diagnosis of myocardial infarction.
- 20 22. The method according to claim 17 or 18, wherein said effective amount of an NF- κ B p65 inhibitor is administered locally to the heart within 2 hours, preferably within 1 hour, more preferably within 0.5 hours from the reperfusion of the heart following removal of an obstruction in a coronary artery.
- 25 23. The method according to claim 17 or 18, wherein said effective amount of an NF- κ B p65 inhibitor is administered locally to the heart substantially at the time of reperfusion of the heart following removal of an obstruction in a coronary artery.
24. The method according to any one of the claims 17 – 23, wherein the antisense NF- κ B p65 subunit oligonucleotide is chosen from the group consisting of SEQ ID NO. 1, SEQ ID NO. 2, and functionally equivalent homologues thereof.

25. The method according to any one of the claims 17 – 23, wherein the antisense NF- κ B p65 subunit oligonucleotide is SEQ ID NO. 2.
26. The method according to any one of the claims 17 – 23, wherein the amount of antisense NF- κ B p65 subunit oligonucleotide administered to the mammal is about 100 μ g to about 5 mg per g/kg body weight.
27. The method according to any one of the claims 17 – 23, wherein the ischemia is the result of vascular occlusion of a cardiac vessel.
28. The method according to any one of the claims 17 – 23, wherein the ischemia is the result of angioplasty.
29. The method according to any one of the claims 17 – 23, further comprising the step of administering at least one second agent selected from the group consisting of anticoagulants and anti-thrombotics, such as vitamin K-antagonists, heparin and heparinoid agents, platelet aggregation inhibitors and the like.
30. The method according to any one of the claims 17 – 23, wherein said NF- κ B p65 inhibitor is a siRNA construct.
31. The method according to claim 30, wherein the siRNA construct is directed towards one of the target sequences given in Table 1.
32. The use of an NF- κ B p65 inhibitor for the manufacture of a pharmaceutical composition for preventing, reducing the extent and/or the severity of secondary ischemic damage in a mammalian organ or tissue.
33. The use of an NF- κ B p65 inhibitor for the manufacture of a pharmaceutical composition for protecting tissue adjacent to area of myocardial infarct in a mammal.
34. The use of an NF- κ B p65 inhibitor for the manufacture of a pharmaceutical composition for preventing, reducing the extent and/or the severity of reperfusion ischemia in a mammalian organ or tissue.

35. The use of an NF- κ B p65 inhibitor for the manufacture of a pharmaceutical composition for preventing, reducing the extent and/or the severity of secondary myocardial infarct resulting from coronary ischemia in a mammal.
- 5 36. The use of an NF- κ B p65 inhibitor for the manufacture of a pharmaceutical composition for preventing, reducing the extent and/or the severity of secondary myocardial infarct resulting from vascular occlusion of a cardiac vessel.
- 10 37. The use of an NF- κ B p65 inhibitor for the manufacture of a pharmaceutical composition for preventing, reducing the extent and/or the severity of secondary myocardial infarct resulting from angioplasty.
- 15 38. The use of an NF- κ B p65 inhibitor for the manufacture of a pharmaceutical composition for preventing, reducing the extent and/or the severity of ischemic brain injury.
- 20 39. The use according to any one of claims 32 – 38, wherein said NF- κ B p65 inhibitor is chosen from the group consisting of: small molecular inhibitors; an antisense NF- κ B p65 subunit oligonucleotide; a dominant-negative form of the NF- κ B p65 subunit; a decoy; ribosome inhibition; enzymatic RNA against NF- κ B; and siRNA constructs.
40. The use according to any one of claims 32 – 38, wherein said NF- κ B p65 inhibitor is an antisense NF- κ B p65 subunit oligonucleotide.
- 25 41. The use according to claim 40, wherein said antisense NF- κ B p65 subunit oligonucleotide is an antisense compound from 8 to 40 nucleotides in length, targeted to a nucleic acid molecule encoding the NF- κ B p65 subunit or to a fragment or analogue thereof.
42. The use according to claim 40, wherein the antisense NF- κ B p65 subunit oligonucleotide is chosen from the group consisting of SEQ ID

NO. 1, SEQ ID NO. 2, and functionally equivalent homologues thereof.

43. The use according to claim 40, wherein the antisense NF- κ B p65 subunit oligonucleotide is SEQ ID NO. 2.

5 44. The use according to any one of claims 32 – 38, wherein said pharmaceutical composition comprises at least one second agent selected from the group consisting of anticoagulants and anti-thrombotics, such as vitamin K-antagonists, heparin and heparinoid agents, platelet aggregation inhibitors and the like.

10 45. The use according to any one of claims 32 - 38, wherein said NF- κ B p65 inhibitor is a siRNA construct.

46. The use according to claim 45, wherein the siRNA construct is directed towards one of the target sequences given in Table 1.
